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CONTENTS/SUMMARIES

Summary: Although the concept of the nucleus and its role in the hereditary continuity of the plant and animal cell was firmly established in the 19th century, it was not until the 1960s that the essential nature of the bacterial equivalent was discerned. This paper reviews ideas on the bacterial nucleus beginning with cytological work done in the early part of the 20th century and concluding with current ideas that arose out of the emerging field of molecular genetics. Despite extensive cytological work, it was only when the genetic recombination process had been understood that intelligent research on the nature of the bacterial nucleus could be pursued. Ultimately, careful electron microscopic studies, interpreted in the light of bacterial genetics, revealed that a nucleus in the classical sense does not exist in bacteria. The deoxyribonucleic acid of the bacterial genome is a long fibrillar molecule that exists as a gel-like solution of great viscosity. If cells are opened gently, each deoxyribonucleic acid molecule remains as a compact rapidly sedimenting structure that can be equated with a morphologically visible structure now termed the bacterial "nucleoid." With cytological fixation procedures, clumping of bacterial deoxyribonucleic acid into microscopically visible structures occurred. These were erroneously interpreted as nuclei and occasionally as mitotic figures. The bacterial "nucleus" is thus an experimental artefact. The second part of this paper discusses how ideas on the nucleus have influenced bacterial classification. The separation of organisms into two broad groups, the procaryotes and the eucaryotes, is based on the nature of the nucleus. Although the prefix "pro" implies that the bacterial nucleus was the forerunner of the eucaryotic nucleus, molecular phylogenetic studies have suggested a tripartite division of extant life (archaebacteria, eubacteria, and eucaryotes) in which the procaryotes are no more ancient than the eucaryotes. Thus, although the nature of the bacterial nucleus has pervaded thinking about classification for over 100 years, most of the ideas have been unfruitful, based as they have been on improper facts, blind prejudice, and unclear thinking. Molecular phylogeny may ultimately settle questions of bacterial phylogeny without reference to the concept of a morphological nucleus.

Summary: The Leishmania spp. are intracellular protozoal parasites which belong to the family of hemoflagellates that includes the highly infectious and well-known trypanosomes. Organisms of this genus are responsible for one of the major classes of communicable diseases of the world. The flagellated protozoan has a digenic life cycle; in the alimentary tract of its insect vector, the blood-sucking sandfly, it exists extracellularly as the motile promastigote form, whereas in the phagolysosomal system

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of mammalian macrophages, it exists intracellularly as the nonmotile amastigote form. The amastigote has apparently adapted to survive and multiply in an acid environment like that provided by the phagolysosome of polymorphonuclear leukocytes. In contrast, promastigotes perform their metabolic functions optimally at neutral pH. Little is known about the key enzymes involved in the critical phases of the organism's life cycle or in the host-parasite interaction. This review focuses mainly on the enzymes and metabolic machinery of the Leishmania spp. responsible for the various forms of leishmaniasis in humans: visceral leishmaniasis (kala azar), mucocutaneous leishmaniasis, and cutaneous leishmaniasis. We summarize the results of reports which describe the enzymes and proteins that are localized to the outer surface of the various species of Leishmania. Emphasis is placed on the predominant cell surface acid phosphatase which has the ability to inhibit markedly the oxygen burst and the production of O_2^- by stimulated phagocytes. The mechanism of action of the leishmanial acid phosphatase seems to involve reductions in second-messenger levels in phosphatase-treated phagocytes. In addition, this review attempts to consolidate existing knowledge about the properties and possible functions of nucleotidases, proteases, protein kinases, and the glycoproteinaceous excreted factor produced by the Leishmania spp. Finally, we review the metabolic capabilities of the Leishmania spp., including the pathways of carbohydrate, fat, amino acid, purine, and pyrimidine metabolism, keeping in mind their possible significance to the host-parasite relationship.

Summary: The plasmid NR1 is the original IncFII drug resistance (R) plasmid isolated 30 years ago from a strain of Shigella flexneri in Japan by R. Nakaya. In the intervening years, NR1 has become one of the most thoroughly studied bacterial plasmids. NR1 belongs to the IncFII class of antibiotic resistance plasmids, which consists of a group of self-transmissible multiple drug resistance plasmids in bacteria. IncFII R plasmids have sizes near 100 kilobase pairs and are present in their host cells at a low copy number of one to two per bacterial chromosome. Many of the antibiotic resistance genes carried by IncFII R plasmids are contained within several transposable elements that are of interest in their own right. In addition to multidrug resistance, IncFII R plasmids encode functions for the control of their autonomous replication and stable maintenance. A large fraction of the genome of IncFII R plasmids is devoted to promoting self-transmission by bacterial conjugation. These transfer functions are largely homologous to those of the fertility plasmid F. In addition to their medical importance owing to interference in the treatment of bacterial infections, NR1 and its IncFII relatives have been found to be exceptionally interesting subjects for the study of fundamental processes involved in the regulation of bacterial gene expression and deoxyribonucleic acid replication and also for analysis of the process of gene amplification by multiple tandem duplication of segments of the plasmid genome. Approximately 70 genes have now been identified and mapped on NR1 and its relatives. Considering the average sizes of these known genes, the total coding capacity of the NR1 genome is estimated to be between 100 and 300 genes. In this review, the genetic and physical maps of NR1 and its relatives are brought up to date, and each of the known genes and functions of NR1 is briefly discussed.

Summary: It is proposed that, at an early stage of evolution, there were organisms drastically different from anything we know. These organisms were acellular and lacked a mechanism for division, but they could grow. They had neither enzymes nor a mechanism for translation, but they did have an autocatalytic metabolism. They had neither nucleic acids nor any other template, but they possessed inheritance and selection. Although they could barely be called living, they had a capacity for evolution. Central to the proposed theory is the idea that life at this earliest stage consisted of

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autocatalytic chemical reactions confined to an essentially two-dimensional monomolecular organic layer. These surface organisms (surface metabolists) were anionically bonded to positively charged surfaces (e.g., pyrite) at the interface of hot water. The adherence to the positively charged mineral surface is not the result of adsorption (as suggested by Bernal in his clay theory) but of in situ autotrophic growth of anionic constituents acquiring their surface bonding in statu nascendi. Instead of adsorption, the organism is faced with desorption, that is, a selective detachment of its constituents. This means a negative selection favoring higher anionic bonding strength. The theory makes detailed suggestions as to how this early, essentially two-dimensional organism (stage 1) evolves by two distinct later stages: to stage 2, a semicellular organism still supported by its pyrite surface, but with a protective membrane, nucleic acids and enzymes, and an internal broth; and stage 3, a true cellular organism that abandoned its pyrite support and became free to conquer three-dimensional spaces.

Summary: The genes of Salmonella typhimurium LT2 are located on a closed circular linkage map. The original map was determined by interrupted mating in F-mediated conjugation. More recent data are derived primarily from bacteriophage P22- and P1-mediated transduction and from gene cloning and molecular analysis. The circular linkage map is set at 100 U to correspond with the 100-min map of Escherichia coli K-12. In this seventh edition of the linkage map, 750 genes are listed, with 680 of these located on the map and the remaining 70 being genes for which mutant alleles are known or which are cloned but not yet mapped. The linkage maps of S. typhimurium and E. coli K-12 are very similar. A plasmid, pSLT, present in all strains of LT2 except those from which it has been intentionally eliminated can carry mutations which affect the phenotype of the cell. Genetic materials and methods relevant to analysis of S. typhimurium are presented. Wild-type and mutant forms of transposons, primarily Tn5 and Tn10, and bacteriophage Mu enable new approaches to determination of gene expression and to isolation and analysis of genes. A collection of strains carrying transposon insertions around the chromosome of S. typhimurium has been assembled and is available from the Salmonella Genetic Stock Centre. S. typhimurium can be transformed with plasmid DNA by calcium chloride methods or by electroporation. A set of strains carrying F-prime factors with E. coli chromosome fragments, and with Tn10 insertions, is described.

Summary: E. coli and S. typhimurium are very similar in most regards. This is true of their flagellar apparatus and its underlying genetics, which is complex, involving close to 40 genes. In both species, the basic symbol is fla, but for historical reasons the extensions differ widely, bear little relationship to genome order or anything else, and include a number of examples in violation of the well-established convention of Demerec et al. (1). We have developed a new unified nomenclature for the flagellar genes of the two species. The basic symbol fla is abandoned and is replaced by flg for those genes in flagellar region I, flh for those in region II, fli for those in region III, and flj for those in the phase 2 flagellin region of S. typhimurium. Extensions (flgA, flgB, etc.) are given in genome order. The new nomenclature has been incorporated into edition VII of the linkage map of S. typhimurium (see preceding article [3]) and will be incorporated into edition VIII of the linkage map of E. coli to be published shortly.

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*Summary: The life cycle of the budding yeast Saccharomyces cerevisiae has two broad aspects, cell proliferation and transitions between haploid and diploid cell types. Haploids mate to form diploids, and diploids undergo meiosis to form haploids. The life cycle of S. cerevisiae has an additional aspect beyond proliferation, mating, and meiosis: haploid yeast cells (of appropriate genotype) can exhibit a "homothallic" life cycle, one in which a haploid cell can give rise to diploid cells capable of meiosis and spore formation. Yeast strains of other genotypes exhibit a "heterothallic" life cycle, in which a haploid cell is unable to yield diploid cells. Studies of S. cerevisiae have provided a molecular understanding of (i) the different types of yeast cells that participate in mating and meiosis (haploid types **a** and α and the diploid **a**/α cell) and (ii) the mechanism for homothallism. Cell specialization in S. cerevisiae is governed by a master regulatory locus, the mating-type locus (MAT), whose two alleles (MAT**a** and MATα) code for regulatory proteins (one activator and two repressor activities). One of the repressor activities (**a**1-α2) requires products coded by both MAT alleles and thus acts as a molecular monitor for diploidy. These regulatory proteins govern transcription of different gene sets, including **a**-specific genes (expressed only in **a** cells), α-specific genes (expressed only in α cells), and haploid-specific genes (expressed in both **a** and α cells). The homothallic life cycle (ability of haploid cells to produce diploid cells) occurs because of mating-type interconversion: cells first change from one mating type to the other by a programmed genetic rearrangement. Then sibling cells mate to form an **a**/α diploid cell. Mating-type interconversion is thus a process in which the master regulatory locus, MAT, is itself regulated. This review presents an overview of the mating-type locus and how it regulates transcription of other genes, as well as a description of the different methods used for assaying mating and associated phenomena. The molecular mechanism of mating-type interconversion ("cassette" transposition) is summarized, and biological aspects of the switching process, genetic variations that lead to a heterothallic life cycle, and different possible mechanisms for homothallism are discussed. The review concludes with a description of features of the life cycles of other organisms (the fission yeast Schizosaccharomyces pombe, filamentous fungi such as Neurospora crassa, and basidiomycetes such as Schizophyllum commune and Ustilago maydis, as well as ciliates and algae).*

Summary: Cell wall is produced by cells at the expense of considerable energy. Turnover of cell wall may therefore seem to be a costly process, especially if the cell is unable to recycle the turned-over material. So turnover must be considered as part of the overall strategy of growth of the cell. The tension created in the wall by the uptake of nutrients and the biosynthesis of new metabolites must be compensated for by surface expansion. Excision of preexisting wall allows for surface expansion and exposes sites at which new wall materials can be added. Turnover does not necessarily create new acceptor sites for nascent peptidoglycan oligomers, but it can. Newly synthesized peptidoglycan is inserted on the inner wall face near the plasma membrane. When the peptidoglycan becomes cross-linked it assumes tension created by the the turgor pressure of the cell. Incorporation of newer peptidoglycan pushes older wall farther from the plasma membrane. When the peptidoglycan has been pushed to near the wall exterior, it is highly stressed and may be cleaved by autolysins, causing turnover. The clipping of the most highly stressed peptidoglycan by autolysins partially alleviates tension in the wall and allows for surface expansion. So cell growth and wall turnover are tightly coupled in many bacteria. For many microorganisms, turnover is an essential part of cell growth. In this review, surface stress is emphasized as a driving force for cell wall turnover in procaryotes and eucaryotes.

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Summary: The accurate replication and segregation of Saccharomyces cerevisiae chromosomes require participation of at least three cis-acting deoxyribonucleic acid (DNA) elements as well as the numerous proteins that form the replication and segregation complexes. At least some and possibly all chromosomal replication origins can be assayed in plasmids by their ability to direct autonomous replication of plasmid DNA. Function of these autonomously replicating sequences (ARSs) requires an 11-base-pair consensus sequence and flanking DNA. While the proteins that interact with the ARS consensus sequence have not been identified, the genes encoding many proteins necessary for DNA replication are known. These genes have been identified by screening collections of conditional mutants as well as by "reverse genetic" approaches. Chromosome segregation requires binding of the mitotic spindle to chromosomes at their centromere. Functional yeast centromeres are contained within a 120- to 130-base-pair sequence composed of three conserved sequence elements. Isolated fragments of centromeric DNA are being used as tools to isolate proteins that bind to these sequences. Telomeres are dynamic structures that lengthen and shorten during vegetative growth. Several genes that influence telomere length have been identified. The unusual $C_{1-3}A$ repeat found in yeast telomeres is believed to stabilize as well as to facilitate the replication of chromosomal ends. Artificial chromosomes constructed from cloned structural genes, ARS elements, centromeres, and telomeres are 2 to 3 orders of magnitude less stable than natural chromosomes. Chromosome length is clearly an important determinant of chromosome stability, but other, as yet unidentified, elements are almost certainly required for chromosome replication and segregation.

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